-N-(β)-glucuronide can be made.

Synthesis of (±)-*trans*-3'-hydroxycotinine-*O*-(β)-glucuronide

Towards the synthesis of the titled compound, *trans*-3'-hydroxycotinine was synthesized following a literature procedure.[1] The cotinine derivative would be then coupled with a suitable carbohydrate precursor. The synthesis of carbohydrate fragment began by using commercially available glucuronolactone, which was treated with methanolic sodium hydroxide to yield the corresponding methyl ester. The resulting ester was acetylated following the modified literature procedure to give methyl 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranuronate in 40% yield (2 steps). The *O*-acetyl derivative was treated with 30% HBr in acetic acid to afford methyl 2,3,4-tri-*O*-acetyl-1-bromo-1-deoxy-α-D-glucopyranuronate as a single anomer.[2]

The tetraacetyl sugar was then reacted with the cotinine derivative in the presence of a variety of Lewis acids such as $SnCl_4$, TMSOTf, BF_3-OEt_2 under various conditions.[3] The reactions were carried out at various temperatures as well as in different solvents. Variation in amount of Lewis acids was also studied. No coupling reaction was observed although *N*-glycosidation was observed at elevated temperatures. In some cases, the acetate was converted into the orthoester derivative, a known intermediate for Lewis acid catalyzed glycosidation.[4]

Reactions were also tried to couple the acetyl protected α-bromo sugar and the cotinine derivative in the presence of a glycosylation promoter encompassing a variety of silver and mercury salts such as AgOTf, Ag_2CO_3, HgI_2, $Hg(CN)_2$ under different conditions. No desired reaction was observed, and it seemed to us that *N*-glycosidation was predominant if any reaction occurred since the pyridine nitrogen is more nucleophilic than the alcohol.

The unusual low reactivity of glycoside moiety is presumably attributed to the presence of an electron withdrawing 5-carboxylic group, which exerts a destabilizing effect on the incipient carbocation on C-1.[5]

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